REMARKS

Upon entry of the Amendment, claims 1 to 3, 5, and 12 to 18 are pending. Claims 4 and 6 to 11 are canceled without prejudice or disclaimer. Claims 3, 5 and 12 are amended. Claims 13 to 18 are new.

No new matter is added. The amendment to claim 3 adds a period at the end. The amendment to claim 5 corrects the dependency thereof, in view of the cancellation of claim 4. The amendment to claim 12 revises the multiple dependency thereof. New claim 13 corresponds to claim 4, but depends from claim 1. The specification supports new claims 14 to 18, such as on pages 7 to 8 and original claims 6 to 11. Entry of the Amendment is respectfully requested.

I. Claim Rejections – 35 U.S.C. § 101

Claims 6 to 11 are rejected under 35 U.S.C. § 101, allegedly because the claimed invention is directed to non-statutory subject matter.

Referring to page 2 of the Office Action, the Examiner contends that the claims recite a use. Claims 6 to 11 have been canceled without prejudice or disclaimer; therefore, this rejection is rendered moot and it is respectfully requested that it be withdrawn.

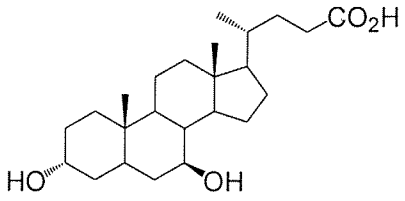
II. Double Patenting

(a) Claims 1 to 12 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 to 11 of U.S. Patent No. 7,138,390 ("the '390 patent"). The Examiner asserts that the claims are not patentably distinct because they both encompass 3, 7-dihydroxy-6-ethyl-5β-cholanic acid. The Examiner admits that the difference between the claims is in the position of the 7-hydroxy group in that the instant claims are drawn to the 7β-isomer of the cited compound. However, the Examiner asserts that both chenodeoxycholic acid and ursdeoxycholic acid are well known bile acids and, thus, the 7β-isomer of the compound of the cited patent is rendered obvious. The Examiner further asserts that the present specification lacks

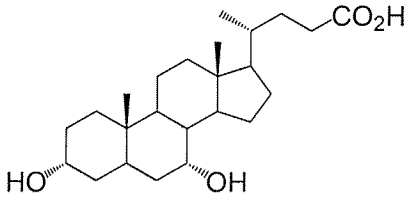
showing of any beneficial property possessed by the claimed 7β-isomer not possessed by the 7α-isomer of the cited patent.

Applicants respectfully traverse this rejection. A person of ordinary skill in the art would not modify the compounds recited in claims 1 to 11 of the '390 patent so that the position of the 7-hydroxy group is in a β configuration. Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *KSR International, Inc. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1741 (2007).

In the present case, no reason has been articulated as to why a person of ordinary skill in the art would have modified the compounds recited in claims 1 to 11 of the '390 patent to possess a 7β configuration. A person of ordinary skill in the art would have appreciated that the 7 position in biliary acid compounds generally provide for significant differences. For example, ursodeoxycholic acid ("UDCA") and chenodeoxycholic acid ("CDCA") possess different properties, given the structural difference in the configuration at the 7-position. UDCA is represented by the following chemical formula:



CDCA is represented by the following chemical formula:



A person of ordinary skill in the art would have appreciated that CDCA is a primary natural bile acid of the human body that amounts to about 40 % of the human bile pool. In stark contrast, UDCA is a tertiary natural bile acid of the human body that amounts to about 3 % of the human bile pool. The difference in the amounts of UDCA and CDCA in the human bile pool indicate that a person of ordinary skill in the art would consider the configuration at the 7-position provide for different properties.

Further, Pellicciari describes that CDCA is a ligand of FXR, but that UDCA is inactive. In this regard, the modification from a 7α configuration to a 7β configuration may provide for significant changes with respect to binding to FXR. Although Pellicciari was disclosed in the Information Disclosure Statement dated on August 25, 2006, a copy is attached for the Examiner's convenience.

Such differences in CDCA and UDCA demonstrate that modifying the 7-position in biliary acids may provide for significant differences in properties. No reason addressing these differences has been identified in the Office Action. In this regard, no reason has been provided as to why a person of ordinary skill in the art would modify the 7α configuration in the compounds recited in claims 1 to 11 of the '390 patent into a 7β configuration.

(b) Referring to pages 3 to 6 of the Office Action, the Office Action includes the following four provisional rejections:

> claims 1 to 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 to 19 of copending Application No. 11/081,002;
>
> claims 1 to 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 24 to 40 of copending Application No. 11/602,307;
>
> claims 1 to 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 to 23 of copending Application No. 11/842,002; and

> claims 1 to 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 to 36, 41, and 43 of copending Application No. 11/914,559.

With respect to Application No. 11/842,002, this application has been abandoned and is therefore no longer co-pending. Therefore, Applicant respectfully requests that the obviousness-type double patenting rejection with regard to Application No. 11/842,002 be withdrawn as moot.

Further, claims 4 and 6 to 11 have been canceled without prejudice or disclaimer; therefore, the provisional rejection with respect to claims 4 and 6 to 11 is rendered moot and it is respectfully requested that it be withdrawn.

Applicant respectfully submits that co-pending U.S. Application Nos. 11/081,002, 11/602,307, and 11/914,559 are currently undergoing examination and respectfully requests that the Examiner hold this provisional obviousness-type double patenting rejection in abeyance, pending a finding of allowable subject matter in these co-pending applications.

Referring to page 6 of the Office Action, the Examiner requests Applicant to provide a complete listing of patents and co-pending patent applications which are "material to the patentability" of the present application. In a sincere effort to advance prosecution, the following co-pending applications are identified: U.S. Application Serial Nos. 11/250,298 and 11/819,517.

III. Claim Rejections – 35 U.S.C. § 112

(a) The Office Action rejects claims 6 to 8 and 11 under 35 U.S.C. § 112, first paragraph, as allegedly not complying with the enablement requirement. The Examiner asserts that the specification does not reasonably provide enablement for prevention. Claims 6 to 8 and 11 have been canceled without prejudice or disclaimer; therefore, this rejection is rendered moot and it is respectfully requested that it be withdrawn.

(b) The Office Action rejects claims 6, 7 and 11 under 35 U.S.C. § 112, first paragraph, as allegedly not complying with the enablement requirement.

Referring to pages 7 to 9 of the Office Action, the Examiner asserts that the specification lacks correlation between activation of farnesoid X receptors and the treatment/prevention of the scope of diseases encompassed by the claims. Claims 6, 7 and 11 have been canceled without prejudice or disclaimer. New claim 14 recites the FXR mediated diseases or conditions of hypercholesteremia, hyperlipidemia, low HDL-cholesterol, and high triglycerides. New claim 15 recites the cardiovascular diseases of artherosclerosis and hypercholesteremia. New claim 16 recites the cardiovascular disease of artherosclerosis. Accordingly, Applicant believes the new claims are allowable and respectfully requests that the rejection be withdrawn. Applicant further reserves the right to pursue other method claims in a continuation application.

(c) Claims 6, 7 and 11 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 6, 7, and 11 have been canceled without prejudice or disclaimer. New claim 14 recites the FXR mediated diseases or conditions of hypercholesteremia, hyperlipidemia, low HDL-cholesterol, and high triglycerides. New claim 15 recites the cardiovascular diseases of artherosclerosis and hypercholesteremia. Accordingly, Applicant believes the new claims are allowable and respectfully requests that the rejection be withdrawn. Applicant further reserves the right to pursue other method claims in a continuation application.

(d) Claims 3, 6, 7 and 11 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner points out that claim 3 lacks a period at the end. Claim 3 has been amended to include a period; therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner asserts that claims 6, 7, and 11 are indefinite. These claims have been canceled without prejudice or disclaimer. Further, new claim 14 recites the FXR mediated diseases

or conditions of hypercholesteremia, hyperlipidemia, low HDL-cholesterol, and high triglycerides. New claim 15 recites the cardiovascular diseases of artherosclerosis and hypercholesteremia. Accordingly, Applicant believes the new claims are allowable and respectfully requests that the rejection be withdrawn. Applicant further reserves the right to pursue other method claims in a continuation application.

IV. Claim Rejections – 35 U.S.C. § 103

Claims 1 to 12 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Frigerio et al. (EP 312867). Frigerio et al. is relied on in this action for teaching 6-methyl substituted bile acid derivatives such as the 6-methyl derivative of ursodeoxycholic acid (UDCA). Frigerio et al. is also relied on for teaching salts as well as conjugates thereof and for use of the compound in the treatment of biliary calculosis as well as pathological conditions in which the stimulation of biliary flow is required. The Examiner admits that the reference teaches a compound which differs as an adjacent lower homolog from the presently claimed compound; however, the Examiner asserts that the claimed invention would have been obvious to one having ordinary skill in the art because the close structural similarity of the reference compound suggests the claimed compound as one skilled in the art would expect the two compounds to have similar properties. Furthermore, the Examiner cites *In re Henze* for the proposition that the court has held that adjacent homologs are obvious absent a showing of unexpected and unobvious results. This rejection is respectfully traversed.

The compounds of the present invention are not rendered obvious by the 6-methyl UDCA derivatives disclosed in Frigerio et al. Based on the teachings of Frigerio *et al.*, one of skill in the art would not have a reason to synthesize the 6-ethyl substitutes of the present invention, nor would one of skill in the art have had a reasonable expectation of success that this substitution would produce such a potent FXR agonist. Frigerio *et al.* describes biliary acid derivatives characterized by the presence of a methyl at the 6th position. However, Frigerio *et al.*'s reason for introducing methyl at the C-6 derivative was to introduce steric hindrance to the molecule. Frigerio *et al.* were not seeking to produce a potent FXR agonist. In fact, the FXR receptor was not even discovered

until 1999, over 10 years after the filing of the Frigerio *et al.* patent application. Frigerio *et al.* provides no teaching or suggestion that the introduction of a C-6 substituent could have dramatic consequences on the FXR receptor-mediated pharmacodynamic properties of the corresponding derivatives.

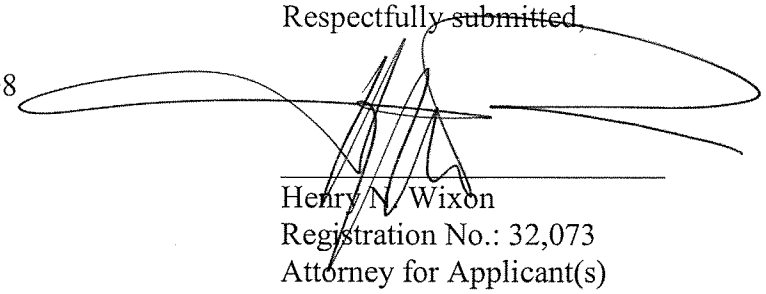
V. Conclusion

In view of the above amendment, Applicant believes the pending application is in condition for allowance. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant herewith petitions the Director of the USPTO to extend the time for reply to the above-identified Office Action for an appropriate length of time, if necessary. Any fee due under 37 C.F.R. § 1.17(a) is being paid via the USPTO Electronic Filing System, or if not paid through EFS, please charge our Deposit Account No. 08-219, under Order No. 0113847.00127US1 from which the undersigned is authorized to draw.

Dated: November 3, 2008

Respectfully submitted,



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